August 26, 1949.

Dr. M. R. Zelle,
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Dear Max:

Most of your old H-168 cultures turned out to be as they should have been, Xyly. Judging from the only other stocks that I have sent you, the Xyl- Mtly type you later got out must have come from H-168; nothing else was Mtly. However, we were unable to reproduce the change from Xyly to Xyl- in some rather extensive tests.

I don't think that there is much more that can be done with H-168. The Xyly to Xyl- change presumably came from a refusion of segregants, but there is no way to prove this. The extremely biassed segregations in H-168 make impossible the desideratum of isolating co-segregants. H-206 should be rather more suitable for this purpose, and I haven't turned up anything better.

Next month we are going to start on the problem of controlling the nuclear condition of E. coli, but I am not very optimistic. We also will try to get under way a general study of the cytology of the diploids, and this may unearth some new ideas. The number of nuclei per cell seems to be variable throughout the growth cycle, but I have been told that the small cells of the decline phase may be uninucleate. However, when growth resumes, cell division already lags behind nuclear division. But it might be worthwhile using such old cells as starting material for a series of isolations if they are technically amenable.

Meanwhile, L. Cavalli (in Fisher's lab at Cambridge) has come out with an interesting development: a derivative of 58-161 (B-M- from K-12) which recombines [i.e. fuses] at an extraordinarily high rate. He is proceeding with a cytological study to try to define the fusion process, but meanwhile, I have been trying to get some data on the segregation genetics, by using his High Frequency of Recombination (Hfr) stock to do crosses on complete medium, tagging segregating zygotes by their sectored appearance on EMB. The zygotes here are not persistent at all, but are formed at a very high rate, constituting under optimal conditions, as much as 1/2 % or so of the <u>total</u> population. If conditions can be found to increase this tenfold or so, it may become feasible to look for the zygotic cells microscopically, and transplant them directly, which would be ideal for genetic analysis. But I suspect that this is precisely what Cavalli intends to do. What I have gotten so far on the genetic analysis jibes very well with conclusions on the heterozygote: All types are <u>not</u> recovered, usually only two, rarely three (2 parentals and one recombinant) types from a single segregating colony [i.e. zygote]. There seems to be the same elimination mechanism which disposes of the Mal+ contribution, that we have seen in the <u>Het</u> diploids which are Mal-/... instead of Mal-/Mal+/ In some ways the Hfr stocks will be more suitable for pursuing that analysis.

Very encouragingly, Cavalli has also found another coli strain (var. acidi-lactici 123 from the Br. Nat. Type Culture Coll) which recombines with K-12. They do not seem to be very much alike in any other respects.

Have a good time fishing,

Sincerely,

Joshua Lederberg